SERVIER INTERNATIONAL

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Direct Healthcare Professional Communication

Important new restrictions for the use of Protelos (strontium ranelate) following new data showing an increased risk of myocardial infarction

Dear Healthcare Professional,

This letter is to inform you of the new contraindications and warnings with Protelos (strontium ranelate).

These measures are intended to reduce the risk of cardiac adverse events which have become evident in a recent routine analysis of safety data from patients taking Protelos.

Summary:

Available data from randomized clinical trials on the cardiac safety of Protelos in the treatment of osteoporosis show an increased risk of serious cardiac disorders including myocardial infarction with no increased risk in mortality observed.

The safety information of the product information has been reinforced as follows:

- **Treatment should only be initiated by a physician with experience in the treatment of osteoporosis, and the decision to prescribe strontium ranelate should be based on an assessment the individual patient's overall risks.**
- **Protelos should not be used in patients with ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease, or a history of these conditions, nor in patients with uncontrolled hypertension.**
- **Further Information:**
  - **Prescribers are advised to assess the patient's risk of developing cardiovascular disease before starting treatment and therefore at regular intervals.**
  - **Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with strontium ranelate after careful consideration;**
  - **Treatment with Protelos should be stopped if the patient develops ischaemic heart disease, peripheral arterial disease, cerebrovascular disease or if hypertension is uncontrolled.**

Merci d'adresser toute correspondance au :
Siège social : 50, rue Carnot • 92284 Suresnes cedex • Tél.: 01.55.72.60.00
S.A.R.L. au capital de 7.995 euros • 321 357 865 RCS Nanterre

Further information on the safety concern:

A recent review of all available safety data for strontium ranelate has raised concern about its cardiovascular safety beyond the already recognized risk for venous thromboembolism. An analysis of randomized controlled trial data has identified an increased risk for serious cardiac disorders, including myocardial infarction (MI) with no observed risk in mortality. This conclusion is predominantly based on data from pooled placebo-controlled studies in post-menopausal osteoporotic patients (3803 patients treated with strontium ranelate, corresponding to 11270 patient years of treatment, and 3769 patients treated with placebo, corresponding to 11250 patient years of treatment). In this data set, a significant increased risk of myocardial infarction was observed in strontium ranelate-treated patients as compared with those given placebo (1.7% versus 1.1%), with a relative risk of 1.6 (95% CI = [1.07; 2.38]). Further, there was an imbalance of more serious cardiac events, including myocardial infarction, associated with strontium ranelate both in a study in osteoporotic men, and in a study in osteoarthritis. In addition, there is a possible mechanistic rationale for an increased risk of serious cardiac disorders including myocardial infarction, given the thrombotic potential for strontium ranelate (Press release EMA/258269/2013).

In order to minimize the risk of MI, the product information has been strengthened as detailed above, with introduction of contraindications and warnings and a recommendation to prescribers to base the decision to prescribe strontium ranelate on an assessment of the individual patient's overall risks.

The letter is sent in agreement with the Saudi Food and Drug Authority.

Call for reporting

As a reminder, there is a need to report any suspected adverse reactions in accordance with the national spontaneous reporting system:

http://www.sfda.gov.sa./en/drug/about/sector_departments/national_pharmacovigilance_center/Pages/reporting_forms.aspx.

Or by email: npc.drug@sfda.gov.sa

Or by fax: +966 1 2057662

Company contact point

For further inquiries concerning this information, please contact the Medical Information Department of SERVIER by phone (+966 2 6976997) and at: samy.sinnuqrut@sa.netgrs.com

Yours sincerely

Alain BARATTA MD
Medical Director N & M East Africa/FOT